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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,380	09/22/2000	Gregory Donoho	LEX-0042-USA	9804

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EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/667,380	GREGORY DONOHO	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Applicants' amendment and response to office action dated June 3, 2003, filed on September 9, 2003 is acknowledged. No prior claims have been amended. New claims 6-9 have been added. Therefore, claims 1-9 are currently pending and are under examination.

Response to Remarks and arguments

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

Claims 1-9 remain/are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The claimed proteins are not supported by either a specific asserted utility or a well established utility because the specification fails to assert any utility for the claimed proteins or the polynucleotides encoding these proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed proteins or the polynucleotides encoding them such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be assessed.

The specification indicates (see page 2-7), that the novel human proteins (NHP), share structural similarity with animal trypsin inhibitor proteins. Additionally the invention contemplates a nucleotide sequence encoding a contiguous NHP open reading frame (ORF), however specification fails to provide any description of the NHP, which has an activity of the trypsin inhibitor protein. Applicants assert (page 2, lines 2-6) that the NHPs described for the

first time herein share structural similarity with animal trypsin inhibitor proteins. Also as such the novel genes represent a new class of proteins with a range of homologues and orthologs that transcend phyla and a range of species. Specification has not provided any percentage similarity of claimed NHPs with any trypsin inhibitor protein or has described or demonstrated a correlation of this structural homology with any function that trypsin inhibitor protein may have. By asserting a protein sharing structural similarity with animal trypsin inhibitor proteins it is intended proteins exhibiting activity similar, but not necessarily identical, to an activity of the animal trypsin inhibitor protein. The specification has not provided any sequence identity of NHPs or percent similarity to the sequence of known member of trypsin inhibitor protein or to the sequence of a member that represents a new class of protein as stated at page 2, lines 4-5. No activity of the claimed protein has been provided in the specification that can be correlated with trypsin inhibitor protein or with the activity of a new class of protein.

A sequence identity search for SEQ ID NO: 1 using GenBank database indicates the alignments and percent similarity to sequences, identified as Accession NOs: AAS60871 (Lillie et al.) and AAD17766 (Vernet et al.). Lillie et al. (US 2002/0110815 A1, August 15, 2002, page 1, col 2) teach a human cancer agent-resistance marker #530, which has 99.8% sequence identity to SEQ ID NO: 1 (see sequence alignment result, N_Geneseq_032802, Accession NO: AAS60871, January 29, 2002), while Vernet et al. (WO 01/62928 A2, August 30, 2001) teach a human novel trypsin inhibitor-like protein, NOV-4b and NOV-4d (see page 1, Table 1, page 82, 83, 87 and 88), wherein DNA encoding NOV-4D is having 98.9% sequence identity to SEQ ID NO: 1 (see sequence alignment result, N_Geneseq_032802, Accession NO: AAD17766, December 10, 2001).

A sequence identity search for SEQ ID NO: 2 using GenBank database indicates the alignments and percent similarity to sequences, identified as Accession NOs: Q9H0B8 (Wambutt et al.) and AAE10616 (Vernet et al.). Wambutt et al. teach a human hypothetical 55.9 kDA protein, which has 99.9% sequence identity to SEQ ID NO: 2 (see sequence alignment result, SPTREMBL_19, Accession NO: Q9H0B8, March 1, 2001), while Vernet et al. (WO 01/62928 A2, August 30, 2001) teach a human novel trypsin inhibitor-like protein, NOV-4b and NOV-4d (see page 1, Table 1, page 82, 83, 87 and 88), wherein protein NOV-4B is having 99.4%

sequence identity to SEQ ID NO: 2 (see sequence alignment result, A-Geneseq_032802, Accession NO: AAE10616, December 10, 2001).

Thus, the foregoing indicates that the sequence of SEQ ID NO: 1 and 2 of the instant application have a lower percent similarity (98.9 and 99.4% respectively) to the nucleic acid and protein sequence of Vernet's trypsin inhibitor-like protein, while the instant sequence of SEQ ID NO: 1 and 2 demonstrate a relatively higher percent similarity (99.8% and 99.9% respectively) to the nucleic acid and protein sequence of Lillie's cancer agent-resistance marker and Wambutt's hypothetical protein respectively. Lillie's markers can be used to determine the sensitivity or resistance of cancer cells to a therapeutic agent, furthermore the markers can be used in selecting appropriate treatment agents (please see page 1, col 1 to col 2, paragraph 0006). Lillie's cancer agent resistance-marker or the selected therapeutic agent using these markers do not describe any activity of trypsin inhibitor-like protein. Therefore, one of skill in the art would question that the protein has been placed in the correct family of protein i.e. trypsin inhibitor-like protein as is asserted. The search result indicates that the claimed protein more likely belongs to a family other than that asserted i.e. a cancer agent-resistance marker. The specification fails to disclose any property and biological activity of NHPs which share the specified activities of trypsin inhibitor-like protein. The artisan would need to prepare, isolate and analyze the protein in order to determine its function and use, thus the utility is not substantial. Therefore, only on the basis of sequence similarity it cannot be interpreted that NHPs protein would have similar activities of trypsin inhibitor-like protein family proteins. The utility cannot be extrapolated from family.

Based on the specification (pages 2-7), any biological activity of the nucleic acid and encoded polypeptide itself has not been provided. However, generalized statements regarding uses have been provided on pages 2-13 of the specification, but are discussed in the context of being used for further research, but to do what? The function/biological activity of the protein is not per se set forth in the instant specification. One skilled in the art should not have to engage in discovering genomics to learn how to use the invention. Therefore, the utility of NHPs encoded by a nucleic acid that shares structural similarity with animal trypsin inhibitor proteins is not a substantial utility because there is no real world context in which to use a protein having no known activity. This situation requires carrying out future additional research to identify or

reasonably confirm a "real world" context of use and therefore do not define specific and substantial utility.

Other activities that the protein may exhibit are listed throughout pages 8-15 of the specification. The specification at page 8 indicates that suitably labeled NHP nucleotide probes can be used to screen a human genomic library, the identification and characterization of human genomic clones is helpful for identifying polymorphisms, determining the genomic structure of a given locus/allele and designing diagnostic tests. Also, the specification describes at page 11-12 that NHPs or NHP peptides, NHP nucleotide sequences can be useful for the detection of mutant NHPs or inappropriately expressed NHPs for the diagnosis of disease. Further, the specification asserts that the NHP proteins or peptides, NHP fusion proteins, NHP nucleotide sequences, host cell expression system and genetically engineered cells and animals can be used for screening for drugs (or high throughput screening of combinatorial libraries) effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body. There are no teachings provided in regards to identifying polymorphisms or use of inappropriately expressed NHPs for the diagnosis of diseases or use of genetically engineered cells for drug screening. At page 13, lines 12-15 specification indicates that in addition to the genes encoding trypsin inhibitors, the described NHPs share significant similarity to a variety of cancer pathogenesis proteins, sperm glycoproteins, and secretory proteins. However, the specification fails to provide any activity of NHPs that can be correlated with the activity of these proteins. Therefore, these utilities are not substantial utilities because there is no real world context to use these polynucleotides and polypeptides without further research to confirm this utility. The utilization of NHP genes and its product in gene therapy and other therapeutics have been described in pages 12-13. However, generalized statements regarding the activity of the gene product are set forth at pages 12-13. In summary, the polypeptides claimed do not have a credible, specific or well-established or even demonstrable utility and therefore lacks utility under 35 U.S.C. 101.

In the instant case, the failure of the specification to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the protein set forth in SEQ ID NO: 2 or for

the polynucleotides of SEQ ID NO: 1 encoding the protein other than the fact that the protein may have a similar activity of trypsin inhibitor-like protein (p. 2). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 2 based on its structure alone for the reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

The rejection has been set forth in the previous office action. In response, applicants traverse the foregoing rejection and argue (pages 4-13) that the present invention has a number of substantial and credible utilities, for example diagnostic tests, such as forensic analysis (page 5). Applicants indicate that at page 13 of specification the described open reading frames can also contain several polymorphisms in SEQ ID NO: 1 and SEQ ID NO: 3. Applicants argue that the present sequences must in themselves be useful because as such polymorphisms are the basis of forensic analysis, which is a "real world" utility. Applicants arguments are not found persuasive because the description of such polymorphisms does not appear in the specification. Further, Applicants urge (page 5) that using the polymorphic markers one can distinguish the members of a population, each marker is useful to distinguish 50% of the population. However, the specification fails to describe or demonstrate that in the real world context. Therefore, the claimed invention is not supported by a well established, credible, specific and substantial asserted utility.

In response to Applicants' citation of *Carl Zeiss Stiftung v. Renishaw*, the Applicants have stated the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S,C. 101, should not be confused with the requirement for a **unique** utility, which is clearly an improper standard. Applicants should note that it is stated in *Carl Zeiss Stiftung v. Renishaw* that "An invention need not be the best or only way to accomplish a certain result..." Applicants have argued further on the issue of specific utility vs. unique utility at page 6. In response it

should be noted that the rejection was on the basis of lack of specific utility, not that the requirement was an unique utility as stated in the response (please see previous office action).

In response to Applicants' citation of *In re Brana* the court indicated that the..."evidence that compounds within scope of claims, and other structurally similar compounds, are effective as chemotherapeutic agents in animals would be sufficient to convince one skilled in art of asserted utility"...Applicants should note that Brana has no correlation with the reasons given for 101 rejection because in the instant case Applicants' assertion of utility is on the basis of structural similarity with trypsin inhibitor like protein. The specification fails to describe any activity that would correlate with the protein of Vernet et al., which has relatively lower percentage sequence identity with the protein claimed. Therefore, how it would be sufficient to convince one skilled in art of asserted utility?

In response to Applicants' citation of *In re Langer* the Applicants have quoted " an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 USC 101." However, Applicants should note that further it is stated in *In re Langer* that " unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." (see MPEP at 2100-30 and *In re Langer*). Therefore, Langer is unpersuasive because in the instant case Applicants assert (page 2, lines 2-6) that the NHPs described for the first time herein share structural similarity with animal trypsin inhibitor proteins. Applicants' assertion of utility is on the basis of structural similarity. It was stated in the previous office action (and also above) that specification has not provided any percentage similarity of claimed NHPs with any trypsin inhibitor protein or has described or demonstrated a correlation of this structural homology with any function that trypsin inhibitor protein may have. Therefore, this reason is sufficient for one skilled in the art to question the objective truth of the statement of utility.

Applicants also point out at page 9, paragraph 1, that the Examiner has presented no evidence to disprove Applicants' asserted utilities for trypsin inhibitor like protein. As for Lillie and Wambutt references Applicants assert that neither of these references supports the Examiner's allegation that the presently claimed sequences is not a trypsin inhibitor like protein, at the same time Applicants assert that given the Vernet et al. disclosure, those skilled in the art

would clearly believe that Applicants' sequence is a trypsin inhibitor like protein. Applicants arguments are not persuasive because it has been stated in previous office action and restated above that the specification fails to disclose any property and biological activity of NHPs which share the specified activities of trypsin inhibitor-like protein. There is no evidence given in the specification in support of the assertion that would lead a skilled artisan to believe that Applicants' sequence is a trypsin inhibitor like protein. Therefore, the claimed invention is not supported by a well established, credible, specific and substantial asserted utility.

Applicants' comments regarding the new utility guidelines set forth by "the PTO" for compliance with 35 U. S. C. 101; the current rules and regulations regarding the examination of patent applications as set forth by USPTO in "MPEP" have been used to assess the current application as required. The commentary regarding other applications and claims is not commensurate to the current application facts.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
January 23, 2004

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